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10/728,196	12/04/2003	Orapin P. Rubino	1289-002US1	7287

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EXAMINER
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1618	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/728,196	RUBINO ET AL.	
	Examiner	Art Unit	
	GiGi Huang	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 December 2003*.

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-34* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:

   I. Claims 1-14 and 30-34, drawn to dosage form comprising an inner and outer zone.

   II. Claim 15, drawn to a method of manufacture capable of utilizing materially different machines from Group III (horizontal rolling granulation verses vertical/"axial" operating apparatus.

   III. Claims 16, 18(a), 18(b), 19-29 drawn to a method of manufacture with a vertical rotor axis and feeding a biologically active agent with binders or an inert powder for an outer surface.

Restriction for examination purposes as indicated is proper because all these inventions listed in this action are independent or distinct for the reasons given above and there would be a serious search and examination burden if restriction were not required because one or more of the following reasons apply:

(a) the inventions have acquired a separate status in the art in view of their different classification;

(b) the inventions have acquired a separate status in the art due to their recognized divergent subject matter;

(c) the inventions require a different field of search (for example, searching different classes/subclasses or electronic resources, or employing different search queries);

(d) the prior art applicable to one invention would not likely be applicable to another invention;

(e) the inventions are likely to raise different non-prior art issues under 35 U.S.C. 101 and/or 35 U.S.C. 112, first paragraph.

Applicant is advised that the reply to this requirement to be complete must include (i) an election of a invention to be examined even though the requirement may be traversed (37 CFR 1.143) **and (ii) identification of the claims encompassing the elected invention**.

The election of an invention may be made with or without traverse. To reserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the restriction requirement, the election shall be treated as an election without traverse. Traversal must be presented at the time of election in order to be considered timely. Failure to timely traverse the requirement will result in the loss of right to petition under 37 CFR 1.144. If claims are added after the election, applicant must indicate which of these claims are readable on the elected invention.

If claims are added after the election, applicant must indicate which of these claims are readable upon the elected invention.

Should applicant traverse on the ground that the inventions are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the inventions to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

2. If Group I is elected, the following election of species is required:

Claims 1-14 and 30-34 are generic to the following disclosed patentably distinct species:

a. For the inner zone:

i. A single biologically active agent

ii. A single specific polymer

b. For the outer zone:

iii. A single biologically active agent

iv. A single specific polymer

The species are independent or distinct because as disclosed the different species have mutually exclusive characteristics for each identified species. In addition, these species are not obvious variants of each other based on the current record.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed and specific species, including the name (generic and chemical), structure, and in the case of the polymer, whether it is a swellable, non-swellable, or release rate. These are required for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable.

There is an examination and search burden for these patentably distinct species due to their mutually exclusive characteristics. The species require a different field of search (e.g., searching different classes/subclasses or electronic resources, or employing different search queries); and/or the prior art applicable to one species would not likely be applicable to another species; and/or the species are likely to raise different non-prior art issues under 35 U.S.C. 101 and/or 35 U.S.C. 112, first paragraph.

Applicant is advised that the reply to this requirement to be complete must include (i) an election of a species to be examined even though the requirement may be traversed (37 CFR 1.143) **and (ii) identification of the claims encompassing the elected species**, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

The election of the species may be made with or without traverse. To preserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the election of species requirement, the election shall be treated as an election without traverse. Traversal must be presented at the time of election in order to be considered timely. Failure to timely traverse the

requirement will result in the loss of right to petition under 37 CFR 1.144. If claims are added after the election, applicant must indicate which of these claims are readable on the elected species.

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the species unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other species.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which depend from or otherwise require all the limitations of an allowable generic claim as provided by 37 CFR 1.141.

3. If Group II is elected, the following election of species is required:

Claim 15 is generic to the following disclosed patentably distinct species:

a. For the inner zone:

i. A biologically active agent

The species are independent or distinct because as disclosed the different species have mutually exclusive characteristics for each identified species. In addition, these species are not obvious variants of each other based on the current record.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed and specific species, including the name (generic and chemical), and structure. These are required

for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable.

There is an examination and search burden for these patentably distinct species due to their mutually exclusive characteristics. The species require a different field of search (e.g., searching different classes/subclasses or electronic resources, or employing different search queries); and/or the prior art applicable to one species would not likely be applicable to another species; and/or the species are likely to raise different non-prior art issues under 35 U.S.C. 101 and/or 35 U.S.C. 112, first paragraph.

Applicant is advised that the reply to this requirement to be complete must include (i) an election of a species to be examined even though the requirement may be traversed (37 CFR 1.143) **and (ii) identification of the claims encompassing the elected species**, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

The election of the species may be made with or without traverse. To preserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the election of species requirement, the election shall be treated as an election without traverse. Traversal must be presented at the time of election in order to be considered timely. Failure to timely traverse the requirement will result in the loss of right to petition under 37 CFR 1.144. If claims are added after the election, applicant must indicate which of these claims are readable on the elected species.

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the species unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other species.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which depend from or otherwise require all the limitations of an allowable generic claim as provided by 37 CFR 1.141.

4. If Group III is elected, the following election of species is required:

a. This application contains claims directed to the following patentably distinct species in step (d):

i. The dry powder has the same composition as the non-wetted powder in step (a)

ii. The dry powder has a different composition from the non-wetted powder in step (a)

It is noted that there are two different claims listed as claim 18. For restriction purposes, the first claim is 18(a) and the second claim is 18(b). Appropriate correction is required.

The species are independent or distinct because claims to the different species recite the mutually exclusive characteristics of such species. In addition, these species are not obvious variants of each other based on the current record.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, claim 16 is generic.

There is an examination and search burden for these patentably distinct species due to their mutually exclusive characteristics. The species require a different field of search (e.g., searching different classes/subclasses or electronic resources, or employing different search queries); and/or the prior art applicable to one species would not likely be applicable to another species; and/or the species are likely to raise different non-prior art issues under 35 U.S.C. 101 and/or 35 U.S.C. 112, first paragraph.

Applicant is advised that the reply to this requirement to be complete must include (i) an election of a species to be examined even though the requirement may be traversed (37 CFR 1.143) **and (ii) identification of the claims encompassing the elected species**, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

The election of the species may be made with or without traverse. To preserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the election of species requirement, the election shall be treated as an election without traverse. Traversal must be presented at the time of election in order to be considered timely. Failure to timely traverse the requirement will result in the loss of right to petition under 37 CFR 1.144. If claims are

added after the election, applicant must indicate which of these claims are readable on the elected species.

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the species unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other species.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which depend from or otherwise require all the limitations of an allowable generic claim as provided by 37 CFR 1.141.

b. Claims 16, 18(a), 18(b), and 19-29 are generic to the following disclosed patentably distinct species:

i. A biologically active agent

The species are independent or distinct because as disclosed the different species have mutually exclusive characteristics for each identified species. In addition, these species are not obvious variants of each other based on the current record.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed and specific species, including the name (generic and chemical), and structure. These are required for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable.

There is an examination and search burden for these patentably distinct species due to their mutually exclusive characteristics. The species require a different field of search (e.g., searching different classes/subclasses or electronic resources, or employing different search queries); and/or the prior art applicable to one species would not likely be applicable to another species; and/or the species are likely to raise different non-prior art issues under 35 U.S.C. 101 and/or 35 U.S.C. 112, first paragraph.

Applicant is advised that the reply to this requirement to be complete must include (i) an election of a species to be examined even though the requirement may be traversed (37 CFR 1.143) **and (ii) identification of the claims encompassing the elected species**, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

The election of the species may be made with or without traverse. To preserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the election of species requirement, the election shall be treated as an election without traverse. Traversal must be presented at the time of election in order to be considered timely. Failure to timely traverse the requirement will result in the loss of right to petition under 37 CFR 1.144. If claims are added after the election, applicant must indicate which of these claims are readable on the elected species.

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record

showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the species unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other species.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which depend from or otherwise require all the limitations of an allowable generic claim as provided by 37 CFR 1.141.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to GiGi Huang whose telephone number is (571) 272-9073. The examiner can normally be reached on Monday-Thursday 8:30AM-6:00PM EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

GH

MICHAEL G. HARTLEY
SUPERVISORY PATENT EXAMINER

Claims: 1. A pellet which is adapted for use as a core for a pharmaceutical dosage form, said pellet having an inner and an outer zone, said inner zone comprising a biologically active agent and said outer zone comprises a layer which is formed by applying to said inner zone, a substantially dry, free flowing inert powder which forms a non-tacky surface when placed in contact with water.

2. A pellet as defined in claim 1 wherein said free flowing, inert powder is a water insoluble powder.

3. A pellet as defined in claim 1 wherein said free flowing, inert powder is selected from the group consisting of microcrystalline cellulose, dicalcium phosphate, calcium sulfate, talc, an alkali metal stearate, silicon dioxide and calcium carbonate.

4. A pellet as defined in claim 1 wherein the inner zone comprises from 0.1-95wt% of one or more pharmaceutically acceptable binders and or diluents and 99.9-5.0wt% of a biologically active agent.

5. A pellet as defined in claim 1 wherein said outer zone is formed from a powder which forms a non-tacky surface when placed in contact with water and from 0.1-99wt% of a biologically active agent.

6. A pellet as defined in claim 1 wherein said outer zone is formed from a powder comprising microcrystalline cellulose and from 0.1-99wt% of a biologically active agent.

7. A pellet as defined in claim 1 wherein said inner zone additionally comprises one or more components selected from the group consisting of lubricants, disintegrants,

flavors, surfactants, anti-sticking agents, osmotic agents and mixtures thereof.

8. A pellet as defined in claim 1 wherein said outer zone additionally comprises one or more components selected from the group consisting of binders, diluents, disintegrants, lubricants, flavors, surfactants, anti-sticking agents, osmotic agents and mixtures thereof.

9. A pellet as defined in any one of claims 1 or 2 wherein said inner or outer zone comprises a swellable matrix forming polymer.

10. A pellet as defined in any one of claims 1 or 2 wherein said inner or outer zone comprises a non-swellable matrix forming polymer.

11. A pellet as defined in any one of claims 1 or 2 wherein said pellet is provided with a layer comprising a swellable matrix forming polymer and a non-swellable matrix forming polymer.

12. A pellet as defined in any one of claims 1 or 2 having one or more layers which comprise a release rate controlling polymer.

13. A pellet as defined in any claim 8 wherein said swellable polymer is selected from the group consisting of hydroxypropyl methyl cellulose, hydroxypropyl cellulose, hydroxyethyl cellulose and carboxypolymethylene.

14. A pellet as defined in any claim 11 wherein said release rate controlling polymers are selected from the group consisting of ethyl cellulose, methacrylic acid copolymers, cellulose acetate phthalate, hydroxypropylmethylcellulose phthalate,

hydroxypropylmethylcellulose acetate succinate, cellulose acetate trimellitate and polyvinyl acetate phthalate.

15. A process for making pharmaceutical pellets as defined in claim 1 wherein said core or at least one of said layers is formed by (a) contacting powder particles, adhering them to each other and compacting said adhered pellets by a rolling movement, wherein the degree of densification is controlled by the rolling movement; and (b) feeding a sufficient amount of a substantially dry, free flowing inert powder which forms a non-tacky surface when placed in contact with water to provide on said particles an outer zone comprising a layer formed from said substantially dry, free flowing inert powder.

16. A process for making solid pellets which are adapted for use as a pellet core for a dosage form which includes a biologically active agent, said process comprising:
(a) forming a powder mixture which comprises a binder and a biologically active agent;
(b) feeding said powder mixture which is optionally pre-wetted with from 0-60% of a pharmaceutically acceptable diluent, based on the total weight of the powder and the pharmaceutically acceptable diluent, to an operating apparatus which comprises a rotor chamber having an axially extending cylindrical wall, means for passing air through said chamber from the bottom, spray means for feeding a liquid into said chamber, a rotor which rotates on a vertical rotor axis, said rotor being mounted in said rotor chamber, said rotor having a central horizontal surface and, in at least the radial outer third of said rotor, the shape of a conical shell with an outward and upward inclination of between 10° and 80°, said conical shell having a circularly shaped upper edge which lies in a plane which is perpendicular to the rotor axis, feed

ports for introducing said powdered excipient, a plurality of guide vanes having an outer end affixed statically to said cylindrical wall of said rotor chamber above a plane formed by the upper edge of said conical shell of said rotor and an inner end which extends into said rotor chamber and is affixed tangentially to said cylindrical wall of said rotor chamber and having, in cross-section to the rotor axis, essentially the shape of an arc of a circle or a spiral, such that said powdered product which is circulated by kinetic energy by said rotor under the influence of kinetic energy, moves from said rotor to an inside surface of said guide vanes before falling back onto said rotor;

(c) rotating said rotor, while feeding air and spraying a pharmaceutically acceptable liquid into said rotor chamber for a sufficient amount of time to form solid pellets having a desired diameter; and

(d) feeding a sufficient amount of a substantially dry, free flowing inert powder which forms a non-tacky surface when placed in contact with water to provide on said particles an outer zone comprising a layer formed from said substantially dry, free flowing inert powder.

18. A process as defined in claim 16 wherein in step (d) the dry powder has the same composition as the non-wetted powder that is fed in step (a).

18. A process as defined in claim 16 wherein in step (d) the dry powder has a different composition from the composition that is fed in step (a).

19. A process as defined in claim 16 wherein said powder mixture in step (a) comprises a biologically active agent and an inert powder that is selected from the group consisting of microcrystalline cellulose, dicalcium phosphate, calcium sulfate, talc, an alkali metal stearate, silicon dioxide, calcium carbonate and mixtures

thereof.

20. A process as defined in claim 16 wherein the powder mixture in step (a) comprises a biologically active agent and an inert powder that is microcrystalline cellulose.

21. A process as defined in claim 16 wherein the biologically ctive compound is selected from the group consisting of vitamins, nutrients, pharmaceuticals and mixtures thereof.

22. A process as defined in claim 16 wherein the biologically active agent is a pharmaceutically active compound.

23. A process as defined in claim 16 wherein the pharmaceutically acceptable liquid diluent is water.

24. A process for making discrete substantially spherical pellets comprising:

(a) feeding, a powder which comprises a biologically active agent and a binder, said powder being pre-wetted with from 5-60% of a pharmaceutically acceptable liquid diluent, based on the total weight of the powder and the liquid diluent, to an operating apparatus which comprises a rotor chamber having an axially extending cylindrical wall, means for passing air through said chamber from the bottom, spray means for feeding a liquid into said chamber, a rotor which rotates on a vertical rotor axis, said rotor being mounted in said rotor chamber, said rotor having a central horizontal surface and, in at least the radial outer third of said rotor, the shape of a conical shell with an outward and upward inclination of between 10° and 80°, said conical shell having a circularly shaped upper edge which lies in a plane which is perpendicular to the rotor axis, feed ports for introducing said powdered excipient, a plurality of guide vanes having an outer end

affixed statically to said cylindrical wall of said rotor chamber above a plane formed by the upper edge of said conical shell of said rotor and an inner end which extends into said rotor chamber and is affixed tangentially to said cylindrical wall of said rotor chamber and having, in cross-section to the rotor axis, essentially the shape of an arc of a circle or a spiral, such that said powdered product which is circulated by kinetic energy by said rotor under the influence of kinetic energy, moves from said rotor to an inside surface of said guide vanes before falling back onto said rotor; and

(b) rotating said rotor, while feeding air and spraying a pharmaceutically acceptable liquid into said rotor chamber for a sufficient amount of time to form substantially spherical pellets having a desired diameter; and

(c) feeding a sufficient amount of a dry powder which comprises a biologically active agent and a binder or a free flowing inert powder which forms a non-tacky surface in contact with water to form an outer layer on said substantially spherical pellets.

25. A process as defined in claim 24 wherein in step (c) dry powder in an amount that is equivalent to 5 to 35 wt.% of the wetted powder that was initially fed to the apparatus, is added and the apparatus is allowed to run for a period of time to form said outer layer.

26. A process as defined in claim 24 wherein said powder which comprising a biologically active agent includes microcrystalline cellulose and optionally comprises one or more components selected from the group consisting of binders, diluents, lubricants, disintegrants, flavors, surfactants, anti-sticking agents, osmotic agents and mixtures thereof.

27. A process as defined in claim 24 wherein the biologically active compound is selected from the group

consisting of vitamins, nutrients, pharmaceuticals and mixtures thereof.

28. A process as defined in claim 24 wherein the biologically active agent is a pharmaceutically active compound.

29. A process as defined in claim 24 wherein the pharmaceutically acceptable liquid diluent is water.

30. A pharmaceutical dosage form which comprises coated pellets having as a core a pellet as defined in claim 1 and one or more release rate controlling coatings selected from the group consisting of delayed release coatings and sustained release coatings or mixtures thereof.

31. A pharmaceutical dosage form as defined in claim 30 wherein the controlled release coating is a sustained release coating.

32. A pharmaceutical dosage form as defined in claim 30 wherein the controlled release coating is a delayed release coating.

33. A pharmaceutical dosage form as defined in claim 30 wherein the dosage form includes different populations of coated pellets having different controlled release coatings.

34. A pharmaceutical dosage form as defined in claim 30 wherein the dosage form is a hard gelatin capsule.